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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/755,251	01/05/2001	Sergio Abrignani	CHIR-0309	6900

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EXAMINER
WORTMAN, DONNA C

ART UNIT	PAPER NUMBER
1648	15

DATE MAILED: 09/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/755,251	ABRIGNANI, SERGIO	
	Examin r	Art Unit	
	Donna C. Wortman, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/011,910* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1648.

Applicant's election without traverse of Group II, claims 22 and 24, in Paper No. 14 is acknowledged.

Claim 24 was amended and new claims 25-40, which read on the elected invention, were added in Paper No. 14. On further consideration, however, the requirement for restriction under 35 U.S.C. 121 is withdrawn and claims 21 and 23 are rejoined with claims 22 and 24-40. Consequently, claims 21-40 are under examination.

Claims 24 and 31 are objected to because of the following informalities: In each claim, in step (b), "solubilizing" is misspelled. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21, 22, and 23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 21 is drawn to a method of treating a patient; claim 22 is drawn to a composition comprising a protein having a molecular weight of about 24 kd, or a functionally equivalent variant or fragment thereof, and capable of binding to E2 of HCV, in combination with a pharmaceutically acceptable carrier; claim 23 is drawn to a method of making a pharmaceutical composition. The

intended use of the composition of claims 22 and 23 encompasses use as a pharmaceutical for treatment of human HCV infection. The specification does not teach that administration of a protein having a molecular weight of about 24 kD, or a functionally equivalent variant or fragment thereof, and capable of binding to E2 of HCV, in fact is of any therapeutic value to a human subject. The specification speculates at several locations that the HCV-binding protein purified as disclosed could be used therapeutically, but does not provide any factual evidence that the *in vitro* demonstration of HCV binding can be correlated with a beneficial effect if the 24 kD protein, or a functionally equivalent variant or fragment of it, is administered to a human subject. In this regard, Pileri et al. (Science 282:938-941, 1998), cited on PTO 892, published well after applicant's effective filing date, is relevant to the consideration of enablement of a treatment method for HCV infection using the 24 kd protein disclosed by applicant to bind to HCV E2. For example, Pileri et al. state: "Whether virus binding to CD81 is followed by entry and infection in all cell types is not clear, because it is possible that additional factors are required for HCV fusion or infectivity" (page 939, top of third column); and "Identification of the interaction between CD81 and HCV could help to elucidate the pathogenesis of HCV-associated diseases, obtain a small animal model of infection, and develop new therapeutic strategies directed at interfering with virus binding" (page 940, bottom of first column). Given the unpredictability remaining in the field even after the time the invention was made, together with the lack of working examples and the lack of any basis for correlating the *in vitro* examples presented with any beneficial effect to be had by treating a patient with the 24 kD protein as claimed,

the specification cannot be said to enable one of skill in the art at the time the invention was made to practice the claimed invention without undue experimentation.

Claims 21-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a "written description" rejection.

Vas-Cath Inc. v. Mahurka, 19 USPQ2d 1111, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the "written description" inquiry, is "whatever is now claimed" (see page 1117). A review of the language of the claims indicates that the claims are drawn to a genus of proteins comprising a 24 kD protein, functionally equivalent variants, and functionally equivalent fragments, some of which are required to bind to HCV E2 protein.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ 2d 1898, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ 2d 1398-1412, the court held that a generic statement that defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that,

while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling with the scope of the claimed genus. At section B(1), the court states "An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention."

The specification only describes a single species, a 24 kD protein that specifically binds the HCV E2 protein. The disclosure of a single disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus; however, the present claims encompass numerous species that vary substantially from one another and that are not further described, i.e., functionally equivalent variants and fragments of the 24 kD protein. The disclosure defines a functional variant as a chemical modification of the 24 kD protein which may include one or more insertions, deletions, or replaced amino acids, no amino acid sequence is provided and there is no further description of functional variants. The disclosure does not provide any description of a fragment of the protein that is functionally equivalent.

Weighing all factors, one skilled in the art would not recognize from the disclosure that the application was in possession of the genus that comprises a protein having a molecular weight of about 24 kD that specifically binds to the E2 protein of hepatitis C virus and functionally equivalent variants and fragments of the protein. The

specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (see *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claims 21-29 and 35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a protein having a molecular weight of about 24 kD purified by the disclosed procedures that specifically binds HCV E2, does not reasonably provide enablement for any and all functionally equivalent variants or fragments thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Even if all the rejected claims were to be clearly limited to fragments and variants that specifically bind HCV E2 protein, the specification does not disclose making any fragments or variants of the isolated and purified 24 kD protein that have that or any other property, nor does it provide guidance as to which portion of the protein can be varied (to make variants) or which can be dispensed with (to make fragments) such that one of skill in the art would be able to practice the invention throughout the scope of the claims without undue experimentation, based on applicant's specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21, 22, 23, and 24 are indefinite in reciting a "functionally equivalent variant or fragment thereof," since it is not clear what equivalent function is required in order to be encompassed by the cited language.

Claims 21, 22, and 23 are indefinite because it is not clear whether "capable of binding to E2 of HCV" is a required property of the recited variants or fragments, or is only required for the 24 kD protein.

Claims 21, 22, 23 and 24 are indefinite in reciting "capable of binding" since being capable of binding is not necessarily the same as actually binding.

Claim 25 is indefinite in reciting "the functional portion of the transmembrane domain" since neither "the functional portion" nor "the transmembrane domain" finds antecedent in claim 24. In addition, it is not clear what function is required for "the functional portion," it is not clear how much of the 24 kD protein is lacking, and it is not clear what portion of the protein is intended by "the transmembrane domain."

Claim 27 is unclear. The term "hyperexpresses" in claim 27 is a relative term which renders the claim indefinite. The term "hyperexpresses" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. While it is recognized that the specification describes a selection process for MOLT4 cells that express more of the 24 kD protein recited in the

claims than the original MOLT4 line, it is unclear how much additional expression is required in order to be a mammalian cell that hyperexpresses the 24 kD protein.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 22 and 24-40 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Levy et al. 1991 (The Journal of Biological Chemistry 266(22):14597-14602, 1991), cited on PTO 892, attached, taken in light of Levy et al. 1998 (cited on PTO 1449 as Ref. AF) and Pileri et al. (Science 282:938-941, 1998), cited on PTO 892. With respect to claims 22, 24, 25, 30, and 36, the prior art product of Levy et al. 1991, *viz.*, TAPA-1, reasonably appears to be identical to the protein claimed except that Levy et al. 1991 is silent as to the inherent functional characteristic of specifically binding to HCV E2. In re Best, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). Levy et al. 1991 disclose the unglycosylated cell surface protein TAPA-1, which is reported to have an apparent molecular weight of 26-kDa and to be expressed on the surface of many types of human cell lines; Levy et al. 1991 also disclose which portions of the molecule are

transmembrane domains and which are extracellular (see, e.g., Fig. 1). The composition of claim 22 is not distinguished from compositions disclosed by Levy et al. since the combination of a protein and a pharmaceutical carrier represents an intended use. While Levy 1991 does not disclose that the TAPA-1 molecule is capable of binding HCV E2, when interpreted in light of Levy et al. 1998, it is apparent that TAPA-1 and CD81 are the same protein, and from Pileri et al., it is apparent that the capability of binding HCV E2 is an inherent property of TAPA-1 (CD81). With respect to claims 26-29, 31-35, and 37-40, recited in product-by-process format, in the absence of factual evidence to the contrary, the 24 kD protein as claimed is the same as the protein of Levy 1991, regardless of the method by which it was obtained. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith. In re Brown, 459 F.2d 531, 535,173 USPQ 685, 688 (CCPA 1972).

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 22 and 24-40 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 17 of copending Application No. 09/011910. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims 22 and 24-40 are drawn to the same protein and compositions comprising that protein as is claim 17 of Application No. 09/011910, which is drawn to a (kit) composition that does not recite any components except the protein; the instant claims are not distinguished from claim 17 of Application No. 09/011910 since the protein and the composition are the same regardless of their intended use.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 21-23 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7 and 27-31 of copending Application No. 09/509612. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to treatment methods, a pharmaceutical composition and a method of making the pharmaceutical composition that use the same protein as the treatment methods recited in claims 7 and 27-31 of Application No. 09/509612 and thus would have been obvious over the treatment methods of claims 7 and 27-31.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna C. Wortman, Ph.D. whose telephone number is 703-308-1032. The examiner can normally be reached on Monday-Thursday, 7:30-5:00 and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Donna C. Wortman, Ph.D.
Primary Examiner
Art Unit 1648

dcw
September 17, 2002